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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/598,416	WILLMANN ET AL.	
	Examiner	Art Unit	
	Russell S. Negin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Comments

Applicant's amendments and request for reconsideration in the communication filed on 3 November 2010 are acknowledged and the amendments are entered.

Claims 1-10 are pending in the instant application.

Claims 1-10 are examined in this Office action.

Withdrawn Objection/Rejections

The objection to the disclosure for informalities is withdrawn in view of amendments filed to the specification on 3 November 2010.

The rejections of claims 1-10 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn in view of amendments filed to the instant set of claims on 3 November 2010.

The rejection of claims 1-4 and 7-10 under 35 U.S.C. 103(a) as being unpatentable over Christopherson et al. [US Patent 5,944,680; issued 31 August 1999] in view of Winokur et al. [US Patent 5,968,932; issued 19 October 1999] in view of Willmann et al. [Biosilico, volume 1, September 2003, pages 121-124; on IDS] are withdrawn in view of argument on pages 10-12 of the Remarks.

The rejection of claim 5 under 35 U.S.C. 103(a) as being unpatentable over Christopherson et al. in view of Winokur et al. in view of Willmann et al. as above, in

further view of Sugita et al. [US PGPUB 2003/0175350 A1; published 18 September 2003] is withdrawn in view of argument on pages 10-12 of the Remarks.

The rejection of claim 6 under 35 U.S.C. 103(a) as being unpatentable over Christopherson et al. in view of Winokur et al. in view of Willmann et al. as applied above, in further view of Numerical Modeling [Definition of Numerical Modelling, 2000, The Dictionary of Physical Geography] is withdrawn in view of argument on pages 10-12 of the Remarks.

The provisional rejections of claims 1-2, 5-6, and 9-10 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2-7 of copending Application No. 11/917,452 are withdrawn in view of amendments filed to the instant set of claims on 3 November 2010.

The provisional rejections of claims 1-2 and 6 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-12 and 16 of copending Application No. 11/569,449 are withdrawn in view of amendments filed to the instant set of claims on 3 November 2010.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The following rejection is necessitated by amendment:

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Step d of claim 1 recites “outputting of the dosage time profile based on the result in [step] c)” wherein it is unclear as to the antecedent basis of the term “result” (the word “result” is never mentioned in step c of claim 1). In the absence of this antecedent basis, it is interpreted that the “iterative adaptive of the dosage time profile” comprises the “result.” However, even with this assumed interpretation, it is unclear as to which iteration of the numerical adaption “the result" has basis (i.e. the first iteration, the second iteration, the final iteration, etc…). Consequently, the term "the result" in step d of claim 1 is interpreted to refer to any numerical adaption of any iteration in step c of claim 1.

Response to arguments:

This rejection is newly applied.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following rejections are reiterated:

Claims 1-10 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Based upon consideration of all of the relevant factors with respect to the claim as a whole, claim(s) 1-10 are held to claim an abstract idea, and are therefore rejected as ineligible subject matter under 35 U.S.C. 101. The rationale for this finding is explained below.

According to the *Interim Guidance for Determining Subject Matter Eligibility for Process Claims in View of Bilski v. Kappos* (75 FR 43922 at 43927 (27 July 2010)), factors that weigh against the eligibility of a process include no recitation of a machine or transformation, involvement of the machine is merely tangentially related to the performance of the steps, and the claim is a mere statement of a general concept.

Claims 1-10 are drawn to methods for the controlled dosage of a medicament as a function of time. These methods do not transform (either explicitly or inherently) any particular physical article. It is noted that the steps of claim 1 recite “inputting” data, "simulating" data, "iterative numerical adapting" of data, and "outputting" data, these steps recite data manipulation rather physically transforming data.

It is noted that steps a and b of claim 1 have been amended to input dosage time profiles into physiology-based and/or pharmacodynamic computer model modules; also claim 9 has been amended to recite that certain parameters are integrated into the “computer model modules.” It is noted that while paragraph 4 of the specification refers to computer models and Figure 1 of the specification refers to the flow chart of the method, there is no disclosure of what constitutes a computer model module (i.e. hardware or software). In the absence of this description, it is interpreted that "computer model modules" refer to software, and there is no tie of each of steps a and b

to a particular machine. Furthermore, even if "computer model module" were to be considered only hardware, the inputting and outputting steps in steps a and d, respectively, are not considered critical ties; these steps are tangentially related to the performance of the set of claims. Likewise, since the preamble of claim 1 does not specify that the method of controlling a computer-controlled dosage device is related to a critical step of claim 1, this recitation of a computer is also interpreted to be tangentially related to the performance of the process in claim 1.

Furthermore, while claim 10 recites that success of therapy is measured online (i.e. related to a machine), this online measurement of success is not related to any significant method step of the claim; instead, it is insignificant because it only pertains to analyzing results and not to performing the critical steps of generating the required results.

The claims merely recite a general concept of controlling the dosage of a medicament, and not a practical application of such a concept. Consequently, the methods claimed are wholly directed to an abstract idea, and therefore are directed to non-statutory subject matter.

Response to arguments:

Applicant's arguments filed 3 November 2010 have been fully considered but they are not persuasive.

Applicant argues that the amendments to claims 1-10 overcome the instant rejection. This argument is not persuasive because, for the reasons discussed above, the set of claims is still not statutory.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following rejections are newly applied:

35 U.S.C. 103 Rejection #1:

Claims 1-4 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Christopherson et al. [US Patent 5,944,680; issued 31 August 1999] in view of

Winokur et al. [US Patent 5,968,932; issued 19 October 1999] in view of Higenbottam et al. [WO 00/01434; published 13 January 2000] in view of Willmann et al. [Biosilico, volume 1, September 2003, pages 121-124; on IDS].

Claim 1 is drawn to a method for controlling a computer-controlled dosage device for the controlled dosage of a medicament into a body of a patient to be tested as a function of time. The method comprises inputting an indication and substance dependent target profile that indicates a desired effect-time profile and a dosage time profile which describes the dose administered as a function of time into a physiology-based and/or pharmacodynamic computer model module. The method also comprises physiology-based pharmacokinetic and/or pharmacodynamic simulating with a time-variable application profile while taking into account individual anatomical and/or physiological parameters of a body to be treated and substance-specific input parameters of the medicament to be administered within the physiology-based and/or pharmacodynamic computer model module and outputting a simulated time profile. The method also comprises iterative adapting of the dosage time profile until the simulated time profile matches the predetermined target profile. The method additionally comprises outputting of the dosage time profile and controlling of the dosage device according to the dosage time profile.

The document of Christopherson et al. is drawn to a respiratory effort detection method [title]. The method is used to correct breathing patterns of humans with respiratory disorders (focusing on sleep apnea) [abstract, cover figure, and column 1,

lines 13-21 of Christopherson et al.]. The computer control of the dosage of the voltage into the patient is illustrated in Figure 19 of Christopherson et al.

Specifically, normal (i.e. target) respiration profiles (flow of area through the subject over time) are input into Figure 2 of Christopherson et al. Figure 4C of Christopherson et al. illustrates a respiration profile of a subject with sleep apnea. To correct the profile, the apparatus ("dosage device") illustrated in Figure 5 of Christopherson et al. is implanted into the patient. When the respiratory profile of the subject is abnormal (such as in Figure 4C of Christopherson et al.) column 30, lines 30-35 of Christopherson et al. teach that this device administers a dose of voltage that is optimized over several trials (i.e. iterations) to correct the abnormal respiratory profile to maximize agreement with the normal respiratory profile (as output in Figure 4A and Figure 4B of Christopherson et al.).

However, Christopherson et al. does not teach use of a medicament (instead, Christopherson et al. uses dosages of electric voltages to resolve sleep apnea). Also, Christopherson et al. does not teach using simulations to model a diseased subject using physiology-based pharmacokinetic profiling (instead, Christopherson et al. obtained the diseased respiratory profile empirically).

The document of Winokur et al. alternatively inhibits sleep apnea with the medicament of the pharmaceutical salt of 6-methyl-5-oxo-3-thiomorpholinylcarbonyl-L-histidine-L-prolinamide [title and abstract]. Column 3, lines 20-40 of Winokur et al. teach inhalation of Montirelin.

However, Winokur et al. does not teach automated administration of the chemical medicament to the patient.

The document of Higenbottam et al. studies inhalers [title]. In particular, the cover figure and abstract of Higenbottam et al. demonstrate the structure and function of an automated inhaler that administers a chemical to the trachea and lungs [Figure 2 of Higenbottam et al.) as needed.

Christopherson et al., Winokur et al. and Higenbottam et al. do not teach using simulations to model a diseased subject using physiology-based pharmacokinetic profiling (instead, Christopherson et al. obtained the diseased respiratory profile empirically).

The article of Willmann et al. teaches the simulation software "PK-Sim," a physiologically based pharmacokinetic "whole body" modeling algorithm. Specifically, Figure 1 on page 122 of Willmann et al. illustrates that to determine the effect of a medicine on the (in this case) human body, the human body is computationally decomposed into a series of connected boxes, wherein each box represents an organ or bloodpool. Differential equations are used to model the kinetics of the profile of the medicine through the iteratively connected boxes as a function of time using a series of empirically obtained parameters.

With regard to claim 2, the cover figure of Christopherson et al. and Figure 1 of Willmann et al. illustrates that the dosage device and simulation is applicable to

humans. Claim 1 of Winokur et al. indicates that their medicament for sleep apnea is applicable to mammals.

With regard to claim 3, column 2, lines 20-30 of Winokur et al. teach intravenous and oral dosages of Montirelin (6-methyl-5-oxo-3-thiomorpholinylcarbonyl-L-histidine-L-prolinamide) to treat sleep apnea. Additionally, column 3, lines 20-40 of Winokur et al. teaches inhalation of Montirelin.

With regard to claim 4, Figure 1 of Christopherson et al. illustrates the volume and composition of a throat and trachea that are normal. Figure 3 of Christopherson et al. illustrates the volume and composition of a throat and trachea that are diseased with sleep apnea. With regard to claims 8-9, the respiratory profiles in Figures 2 and 4 of Christopherson et al. are measured physiologically by the apparatus anatomically positioned in the human in Figure 5 as the subject breathes (real-time).

With regard to claim 7, the device infused into the human in Figure 5 of Christopherson et al. pumps voltage into the human respiration pathway to correct for abnormal respiration profiles.

With regard to claim 10, the therapy in Christopherson et al. is evaluated by measuring pressure through the measurement probe of a pressure sensor (Figure 6 of Christopherson et al.) to determine the signal of intensity of air flow. Additionally, the

resultant signal (whether it be normal as in Figure 2 of Christopherson et al. or abnormal as in Figure 4C of Christopherson et al.) controls whether the dosage of voltage in given by the apparatus to clear the pathway.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the implanted device that applied voltages to treat sleep apnea as in Christopherson et al. by use of administering the medicament Montirelin as in Winokur et al. wherein the motivation would have been that the use of the pharmaceutical in Winokur et al. is non-invasive (i.e. no devices need to be implanted- column 2, lines 20-30 of Winokur et al. and column 3, lines 20-40 of Winokur et al. as compared with Figure 5 of Christopherson et al). There would have been a reasonable expectation of success in combining Christopherson et al. with Winokur et al. because both studies pertain to applying optimized dosages (i.e. electricity or chemicals) for treating sleep apnea when abnormal breathing patterns occur. In addition, it has been shown in Higenbottam et al. that there is success in automated dosing of chemicals to the trachea and lungs [Figures 1 and 2 of Higenbottam et al.].

It would have been further obvious to someone of ordinary skill in the art at the time of the instant invention to modify the invasive and noninvasive approaches of administering dosages in Christopherson et al., Winokur et al., and Higenbottam et al., by use of the computational simulation for the "whole body" as in Willmann et al. wherein the motivation would have been that computational simulation of dosage performance eliminates the need to administer dosages to a subject- invasively or

noninvasively- until optimized conditions have been modeled [Figures 1 and 2 of Willmann et al.]. There would have been a reasonable expectation of success in combining the general study of Willmann et al. to the specific assessment of sleep apnea in Christopherson et al., Winokur et al., and Higenbottam et al. because as the simulations of Willmann et al. are applicable to the "whole body "[title], and the throat and trachea are parts of the body, Willmann et al. provides generally applicable simulated results to the documents of Christopherson et al. and Winokur et al.

Response to arguments:

Applicant's arguments filed 3 November 2010 have been fully considered but they are not persuasive.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Specifically, applicant argues that one of ordinary skill in the art at the time of the instant invention would not have chosen the document of Christopherson et al. as a starting point as being the closest state of the art. This argument is not persuasive

because Christopherson et al. teaches (as an empirical method rather than a simulation) modifying a diseased profile using a treatment to match a target (normal or undiseased) profile. Instead of using a chemical as a medicament, Christopherson et al. uses applied voltages as a "medicament." Consequently, to answer applicant's questions on page 10 of the Remarks, the target profile is the breathing (i.e. from the lungs) profile unaffected by sleep apnea in Figures 4A and 4B of Christopherson et al. Thus, it is the goal of Christopherson et al. to convert the measured profile (affected by sleep apnea- Figure 4C of Christopherson et al.), to become normal again.

Applicant argues that there would have been no reasonable expectation of success in combining a drug (such as Montirelin in Winokur et al.) with the use of electronic voltage drops as in Christopherson et al. This argument is not persuasive because it is noted that there would have been a reasonable expectation of success in substituting a chemical medicament (i.e. the Montirelin of Winokur et al.) for the "electrical" medicament of Christopherson et al. because both forms of medicaments have been proven successful in treating sleep apnea. The document of Higenbottam et al. even demonstrates success of automated inhalers wherein chemicals are automatically delivered to the trachea and lungs of a patient.

Applicant argues that the combination of Christopherson et al., Winokur et al. and Willmann et al. gives a "yes/no" answer to the question of whether an application of a drug is needed based on comparison of measured vs. target profiles. Applicant argues that rather than giving a binary answer to whether a drug is needed, the instant claims control (by a computer) the dosage of a drug necessary to meet the target profile. This

argument is not persuasive because the interpretation of the claims does not exclude a "yes/no" answer of whether a application of a drug will cause a measured profile to match a desired profile. Even assuming (*en arguendo*) this "yes/no" interpretation of the claim not to be valid, Christopherson et al. does not only give a "yes" answer as to the success of using voltages to match a measured profile with a target profile, but Figures 4 and 19 of Christopherson et al. teach when to apply these voltages (using a computer) to optimize the matching of the measured to target breathing profiles. There would have been a reasonable expectation of success in applying the simulation software of Willmann et al. to the empirical studies of Christopherson et al., Winokur et al., and Higenbottam et al. because the PBPK modeling of Willmann et al. is generally applicable to simulating dosage studies (such as Christopherson et al., Winokur et al., and Higenbottam et al.).

Applicant argues that one of ordinary skill in the art would not have been motivated to modify the "yes/no" diagnostic test of Christopherson et al. into a computer controlled dosage device wherein there is iterative modification of the dosages until the measured and target profiled match. This argument is not persuasive because Christopherson et al. iteratively optimizes the dosages of voltages to a patient as a result of previous breathing patterns to assist a measured breathing pattern (Figure 4C and column 30 of Christopherson et al.) to become an target breather pattern (Figures 4A and 4B of Christopherson et al.).

<u>The following rejection is newly applied</u>:

35 U.S.C. 103 Rejection #2:

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Christopherson et al. in view of Winokur et al. in view of Higenbottam et al. in view of Willmann et al. as applied to claims 1-4 and 7-10 above, in further view of Sugita et al. [US PGPUB 2003/0175350 A1; published 18 September 2003].

Claim 5 is further limiting accounting for the substance specific parameter of free fraction of the medicament in plasma.

The documents of Christopherson et al., Winokur et al., Higenbottam et al. and Willmann et al. make obvious methods for determining the controlled dosage of a medicament, as discussed above. The abstract of Winokur et al. teaches use of the drug Montirelin to treat sleep apnea.

The documents of Christopherson et al., Winokur et al., Higenbottam et al., and Willmann et al. do not teach the property of free fraction of the Montirelin in blood plasma.

The document of Sugita et al. teaches preparation and characterization of thyrotropin-releasing hormones and their derivatives [title, abstract]. Paragraph 5 of Sugita et al. teaches that Montirelin is a derivative of thyrotropin-releasing hormones. Paragraph 49 of Sugita et al. teaches the process for measuring blood plasma levels of thyrotropin-releasing hormones and their derivatives.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the empirical and computational determination of controlled dosage of Christopherson et al., Winokur et al., Higenbottam et al., and

Willmann et al. by use of the blood plasma measurement techniques for Montirelin in Sugita et al, wherein the motivation would have been that the result of Sugita et al. yields information on how much Montirelin is capable of dissolving in the bloodstream.

Response to arguments:

Applicant's arguments filed 3 November 2010 have been fully considered but they are not persuasive.

Applicant argues that the reference of Sugita et al. does not overcome the alleged deficiencies of Christopherson et al., Winokur et al., Higenbottam et al., and Willmann et al. This argument is not persuasive because the combination of Christopherson et al., Winokur et al., Higenbottam et al., Willmann et al., and Sugita et al. makes obvious all of the limitations of the instantly rejected claim.

The following rejection is newly applied:

35 U.S.C. 103 Rejection #3:

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Christopherson et al. in view of Winokur et al. in view of Higenbottam et al., in view of Willmann et al. as applied to claims 1-4 and 7-10 above, in further view of Numerical Modeling [Definition of Numerical Modelling, 2000, The Dictionary of Physical Geography].

Claim 6 is further limiting wherein numerical optimization methods comprise gradient and stochastic methods.

The documents of Christopherson et al., Winokur et al., Higenbottam et al., and Willmann et al. make obvious methods for determining the controlled dosage of a medicament, as discussed above. Figure 1 of Willmann et al. suggests a system of differential equations needed to model the pharmacokinetics of a medicament when administered to the body.

The documents of Christopherson et al., Winokur et al., Higenbottam et al., and Willmann et al. do not teach gradient and stochastic methods for optimizing dosages.

The article on Numerical Modeling teaches that gradients and stochastic analyses forms of techniques used to model differential equations [see definition].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the empirical and computational determination of controlled dosage of Christopherson et al., Winokur et al., Higenbottam et al. and Willmann et al. by use of the mathematical techniques in Numerical modeling because it is obvious to combine known elements in the prior art to yield a predictable result. In this instance, the stochastic and gradient techniques are alternate techniques used to solve differential equations. There would have been a reasonable expectation of success in combining the techniques of Numerical modeling with the differential equations in the dosage studies of the combination of Christopherson et al., Winokur et al., and Willmann et al. because the Numerical modeling taught in the definition is general for any system of differential equations (including the differential equations on Willmann et al.).

Response to arguments:

Applicant's arguments filed 3 November 2010 have been fully considered but they are not persuasive.

Applicant argues that the reference of Numerical Modelling does not overcome the alleged deficiencies of Christopherson et al., Winokur et al., Higenbottam et al., and Willmann et al. This argument is not persuasive because the combination of Christopherson et al., Winokur et al., Higenbottam et al., Willmann et al., and Numerical Modelling makes obvious all of the limitations of the instantly rejected claim.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The following rejections are newly applied:

Double Patenting Rejection #1:

Claims 1-2, 5-6, and 8-10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of copending Application No. 11/917,452 in view of Christopherson et al. in view of Winokur et al. in view of Higenbottam et al.. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1-2, 5-6, and 8-10 of the instant application are drawn to methods for the controlled dosage of a medicament as a function of time. Claims 1-7 of '452 are drawn more specifically to a device for the time-controlled administration of the anesthetic propofol wherein the embodiments of '452 comprise the embodiments of claims 1-2, 5-6, and 8-10 of the instant application (i.e. target

concentration-time profile, a simulated PBPK concentration-time profile, iteratively fitting the simulated PBPK concentration-time profile to the target concentration-time profile, and transferring the result to a dose device).

In other words, except for the recitation in the instant claims that the method be computer controlled in that the dosages be computer controlled and that the modeling be related to computer modules, the embodiments of claims 1-7 of '452 are a species of the embodiments of claims 1-2, 5-6, and 8-10 of the instant application. The document of Christopherson et al. teaches computer control (Figure 19) of a device that controls administration of voltage dosages to a patient with sleep apnea. Winokur et al. teaches chemical medication for treatment of sleep apnea capable of being inhaled (column 3, lines 20-40 of Winokur et al.). Higenbottam et al. teaches a computerized inhaler wherein medicines are inhaled via automatic control of an apparatus (Figures 1 and 2 of Winokur et al.).

It would have been obvious to modify claims 1-7 of '452 to be computer controlled as in the combination of Christopherson et al., Winokur et al. and Higenbottam et al. wherein the motivation would have been that this combination of Christopherson et al., Winokur et al. and Higenbottam et al. automates the oral/inhaled administration of medicine (i.e. Figure 19 of Christopherson et al., column 3, lines 20-40 of Winokur et al., and Figures 1 and 2 of Higenbottam et al.).

This table demonstrates the line-up between the instant claims and the claims of '452:

Instant claim	Claim(s) of '452

1	1, 4
2	2
5	3
6	5
8	4
9	6
10	7

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The following rejections are newly applied:

Double Patenting Rejection #2:

Claims 1-2 and 6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-18 of copending Application No. 11/569,449. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1-2 and 6 of the instant application are drawn to methods for the controlled dosage of a medicament as a function of time. Claims 11-18 of '449 are drawn to a method for determining optimized dosages and transferring the optimized dosage to a dosage device. The steps of '449 encompass the steps of claims 1-2 and 6 of the instant application (i.e. an a resulting/target concentration-time profile, a simulated PBPK concentration-time profile,

iteratively optimizing the simulated PBPK concentration-time profile such that there is minimum deviation with the resulting/target profile, and transferring the optimized dosage to a dosage device) plus other limitations. In other words, the embodiments of claims 11-12 and 16 of '449 are a species of the embodiments of claims 1-2 and 6 of the instant application.

In other words, except for the recitation in the instant claims that the method be computer controlled in that the dosages be computer controlled and that the modeling be related to computer modules, the embodiments of claims 11-18 of '452 are a species of the embodiments of claims 1-2 and 6 of the instant application. The document of Christopherson et al. teaches computer control (Figure 19) of a device that controls administration of voltage dosages to a patient with sleep apnea. Winokur et al. teaches chemical medication for treatment of sleep apnea capable of being inhaled (column 3, lines 20-40 of Winokur et al.). Higenbottam et al. teaches a computerized inhaler wherein medicines are inhaled via automatic control of an apparatus (Figures 1 and 2 of Winokur et al.).

It would have been obvious to modify claims 11-18 of '452 to be computer controlled as in the combination of Christopherson et al., Winokur et al. and Higenbottam et al. wherein the motivation would have been that this combination of Christopherson et al., Winokur et al. and Higenbottam et al. automates the oral/inhaled administration of medicine (i.e. Figure 19 of Christopherson et al., column 3, lines 20-40 of Winokur et al., and Figures 1 and 2 of Higenbottam et al.).

This table demonstrates the line-up between the instant claims and the claims of '452:

Instant claim	Claim(s) of '452
1	11-18
2	16
6	12

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 8:30 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Russell S. Negin/
Primary Examiner, Art Unit 1631
14 December 2010